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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,453	12/09/2004	Ogari Pacheco	4705-0106PUS1	5587

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EXAMINER	
HUANG, GIGI GEORGIANA	
ART UNIT	**PAPER NUMBER**
1618	

NOTIFICATION DATE	DELIVERY MODE
12/03/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/517,453	PACHECO ET AL.	
	Examiner	Art Unit	
	GiGi Huang	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,8,15-17,19 and 21-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,8,15-17,19 and 21-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The amendment filed September 14, 2007 has been received, entered and carefully considered. The amendment affects the instant application accordingly:

(A) Claims 1-2, 6, 8, 15-17, 19, and 21-35 have been amended.

(B) Claims 3-5, 7, 9-14, 18, 20, and 36 have been cancelled.

(C) Lines 1-4 on Page 1 in the specification has been amended.

(D) Comments regarding Office Action have been provided drawn to:

a. 103(a) rejection, of Lipari et al. (U.S. Pat. # 6,232,333) in view of Bailey et al. (U.S. Pat. # 6,008,228) has been maintained for the reasons of record.

b. 103(a) rejection, of Lipari in view of Bailey as applied to claims 1-21 above, and further in view of CUBoulder Organic Chemistry Undergraduate Courses, Lab Techniques has been maintained for the reasons of record.

c. 112, Second Paragraph rejection for claims 26-36, for indefiniteness with respect to the methods of manufacture that do not state a specific concentration, weight, or final product form as an endpoint which have been maintained for the reasons of record.

d. 112, Second Paragraph rejection for claims 26-36, directed to the term "appropriate amounts for the composition" which has been deleted by amendment, and withdrawn for the reasons of record.

e. 112, Second Paragraph rejection for claims 26-36, directed to the term "keeping stirring until complete mixture " which has been deleted by amendment, and withdrawn for the reasons of record.

f. Claim objections to claims 22-25 for improper multiple dependence, have been withdrawn for the reasons of record.

2. Claims 1-2, 6, 8, 15-17, 19, 21-35 are pending in the case.

3. Claims 1-2, 6, 8, 15-17, 19, 21-35 are present for examination.

4. The text of those sections of title 35.U.S. Code not included in this action can be found in the prior Office action.

Specification

5. Lines 1-4 on Page 1 in the specification have been amended and are supported.

6. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d) (1) and MPEP § 608.01(o). Correction of the following is required: There is no support in the specification for the compositions to be employed in veterinary use, as set forth in claim 25.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipari et al. (U.S. Pat. # 6,232,333) in view of Bailey et al. (U.S. Pat. # 6,008,228).

Lipari et al. teaches a composition of proteinase inhibitors, specifically ritonavir, that have increased bioavailability. The composition is comprised of a protease inhibitor (ritonavir), fatty acids (organic solvent), alcoholic solvents, surfactants, and antioxidants.

The preferred ranges for the proteinase inhibitor (ritonavir) are from about 1 to about 50% (Col.8, lines 64-68, Col.9, lines 1-17, Col. 10, lines 25-55, Col. 30, Example 35) fulfilling the claims.

The fatty acids (organic solvent) would be utilized in the preferred range of about 20% to about 99%, preferably about 30% to about 70%, and most preferably from about 40% to about 60%.

The alcoholic solvents used include ethanol, propylene glycol, benzyl alcohol, polyethylene glycol 200, polyethylene glycol 300, polyethylene glycol 400/PEG400 (also an emulsion stabilizer), and mixtures thereof. Specifically a mixture of ethanol and propylene glycol preferably from about 10 to about 15% (Col. 8, lines 26-35, Col. 9, lines 17-43 and 60-68, Col. 10, lines 25-55, Col. 30, Example 35).

The surfactants taught included polyoxyl 35 castor oil (Cremophor ® EL), polyethylene glycol 40 hydrogenated castor oil (Cremophor ® RH 40), Tween ® 20, 40, 60, and 80 (polysorbates/polyoxythylene (20) sorbitan mono fatty acid esters). The preferred range for the surfactants taught are from about 0% to about 20%, preferably from about 5 to about 10% (Col. 8, lines 35-63, Col. 9, lines 30-36, Col. 10, lines 25-55). Thereby, the limitations of the claims have been met.

The antioxidants taught include BHT (butylated hydroxytoluene) and ascorbic acid, which is also a polarity corrector, in a preferred range of about 0.01% to about

0.08% (Col. 8, lines 8-12, Col.11, lines 33-40). Lipari also teaches the composition to be encapsulated in a soft elastic gelatin capsule (SEC) or a hard gelatin capsule. It is noted that the recitation of viral treatment and use in medicine or veterinary situations are recitations of intended use and have no weight in a composition claim as long as the composition is capable of the intended use.

Lipari et al. does not expressly teach the incorporation of a mono/diglyceride mixture.

Bailey et al. teaches the incorporation of monoglycerides and specifically the preferred mixture of medium chain mono/diglycerides C_8-C_{10} for proteinase inhibitor compositions, including ritonavir. Bailey teaches that proteinase inhibitors, being hydrophobic and/or lipophilic have difficulty being absorbed, especially due to crystal forms (polymorphs).

Bailey teaches that certain classes of glycerides used as carriers (organic solvents) for formulation assist in alleviating these inadequacies. In fact they achieve better absorption and enhanced bioavailability with good stability/shelf life over a long period of time. The preferred combination was a mixture of medium chain mono/diglycerides C_8-C_{10} that was commercially available under many names including CAMPUL MCM®. The glycerides are derived from medium chain C_8-C_{10} fatty acids. The desired range for the glycerides for compositions containing about 120mg to about 300mg of proteinase inhibitor was 40-80% by weight (Abstract, Col.2, lines 23-62, Col. 3, lines 5-68, Col. 4, lines 1-45, Col.16, lines 5-68, Col. 17, lines 15-35, Col. 19, lines 45-66, Col.20, lines 20-66, Col.21, lines 15-68, Col. 22, lines 8-41 and 53-68).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the fatty acids for a mixture of medium chain mono/diglycerides C_8-C_{10}, as suggested by Bailey, and produce the instant invention as glycerides are derived from fatty acids, have equivalent, if not more desirable, solvent properties, and are routinely substituted dependent on the desired physical properties of the composition and solubilities of the components (e.g. drug) of the composition.

One of ordinary skill in the art would have been motivated to do this because increase bioavailability and shelf life/stability of a ritonavir composition is desirable since the drug is known to have difficulty with crystal forms, stability, and bioavailability.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

9. Claim objections to claims 22-25 for improper multiple dependence have been amended to depend on specific single claims. The objections are withdrawn.

10. Claims 26-36 are rejected under 35 U.S.C. 112, second paragraph, for indefiniteness with respect to the methods of manufacture that do not state a specific concentration, weight, or final product form as an endpoint.

Applicant's arguments see pages 10-11 filed 09/14/2007 have been fully considered but they are not persuasive. Applicant's arguments against the prior art rejections of record are centered on the assertion that one of ordinary skill in the art would be reasonably apprised of the scope of the invention reading the claims as a whole in the light of the specification.

This is not persuasive as the claims are amended to recite steps one of skill in the art would not know the metes and bounds of the invention as there is no reasonable direction stated in the claims for the amounts used or the recitation of "correcting the final weight" of the composition when there is no specific final weight disclosed in the claims. One would not be apprised of the metes and bounds of the invention as it is directed to make a composition where the specifics of the composition are not recited. For the purpose of prosecution, any amount and endpoint was used as there was not one specific final product result recited in the claims.

In response to applicant's argument that one of ordinary skill in the art would be about to bring a substantial amount of knowledge to the patent and thereby have a fair reading of the disclosure of the specification and the claims, it is noted that the applicant

relies on the interpretation of one of skill in the art which will vary as the specifics are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The rejection of claims 26-36 under 35 U.S.C. 112, second paragraph, for indefiniteness with respect to the methods of manufacture that for not stating a specific concentration, weight, or endpoint for the final product form is maintained.

11. Claims 26-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is directed to the indefinite term "appropriate amounts for the composition".

Applicant's arguments see pages 11-12 filed 09/14/2007 have been fully considered and is moot as the term "appropriate amounts for the composition" has been deleted by amendment.

The rejection of Claims 26-36 under 35 U.S.C. 112, second paragraph, as being indefinite with respect to the term "appropriate amounts for the composition" is withdrawn.

12. Claims 26-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is directed to the indefinite term "keeping stirring until complete mixture ".

Applicant's arguments see pages 11-12 filed 09/14/2007 have been fully considered and is moot as the term "keeping stirring until complete mixture " has been deleted by amendment.

The rejection of Claims 26-36 under 35 U.S.C. 112, second paragraph, as being indefinite with respect to the term "keeping stirring until complete mixture" is withdrawn.

13. Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipari et al. (U.S. Pat. # 6,232,333) in view of Bailey et al. (U.S. Pat. # 6,008,228).

Applicant's arguments see Pages 12-17, filed 09/14/2007, have been fully considered and are not persuasive. Applicant's arguments against the prior art rejection of record are centered on the following: a comparison of each of the pieces of prior art individually against the instant application rather than the combination of the references, that saquinavir and ritonavir are different molecules, that Bailey et al. addresses saquinavir and not ritonavir, that Bailey does not exemplify ritonavir, argument that fatty acids and glycerides have distinct physical-chemical properties and it would not be obvious to combine as suitable solvents for ritonavir.

The arguments are not persuasive as the arguments are not commensurate in scope to the claims and the arguments are to individual aspects of the disclosed art and does not addressed the teachings of the prior art as a whole.

Applicant's argument that Bailey et al. addresses saquinavir and not ritonavir along with not exemplifying ritonavir as they are different molecules is not persuasive. The argument that fatty acids and glycerides have distinct physical-chemical properties

and it would not be obvious to combine as suitable solvents for ritonavir is not persuasive.

It is also noted that the limitations of Claim 2 and dependent claims19 and 21 are optional and do not need to be met.

The teachings of Bailey are addressed as a whole.

Bailey teaches that there are polymorph and crystallization issues with HIV protease inhibitors and that there are concerns for achieving good bioavailability. Bailey teaches that there are certain classes of glycerides are useful as carriers (organic solvents) and assist in alleviating these inadequacies as they achieve better absorption, enhanced bioavailability, good stability, and better self life over time. The particular glycerides that were particularly favorable were a mixture of medium chain mono/diglycerides C_8-C_{10} which are commercially available under many names including CAMPUL MCM®.

The glycerides are derived from medium chain C_8-C_{10} fatty acids. The desired range for the glycerides for compositions containing about 120mg to about 300mg of proteinase inhibitor was 40-80% by weight. This would vary dependent the amount of inhibitor in the composition. The fatty acids in Lipari are organic solvents (carriers) and it would be obvious to try and utilize the glyceride mixture for the fatty acids as a solvent, as they present with better absorption, enhanced bioavailability, good stability, and longer self life.

This especially true as Bailey teaches that a mixture of medium chain mono/diglycerides C_8-C_{10} are compatible with many of the HIV protease inhibitors

including ritonavir (see Col. 17, lines 15-35) and as stated by Applicant, suitable solvents for ritonavir are scarce and one of skill in the art would be motivated to try and incorporate the glyceride mixture for its improved properties with a reasonable expectation of success based on the examples of saquinavir and the disclosure for its dissolution of ritonavir (Abstract, Col.2, lines 23-62, Col. 17, lines 15-35, Col. 19, lines 45-66, Col.20, lines 20-66, Col.21, lines 15-68, Col. 22, lines 8-41 and 53-68).

The comparison of the individual pieces of art is not persuasive as they are not commensurate in scope with the claims. The claim limitations are still met by the art as Lipari still teaches ritonavir, the mixture of alcoholic solvents of ethanol and propylene glycol at preferably about 10% to about 15% (5% each in Col.35, Example 35), the organic solvent at preferably about 30% to about 70% and more preferably about 40% to about 60%, surfactant (e.g. polyoxyl35 castor oil) at preferably about 5% to about 10%, and BHT(antioxidant and polarity corrector) in the desired ranges (Col.8, lines 8-12 and 26-68, Col.9, lines 1-43 and 60-68, Col. 10, lines 25-55, Col.11, lines 33-40, Col. 30, Example 35).

The teachings of Bailey, issues of obviousness, and motivation are addressed above and in the previous action.

From recent case law: "the results of ordinary innovation are not the subject of exclusive rights under the patent laws." (KSR INTERNATIONAL CO. v. TELEFLEX INC. ET AL. 550 U. S. ____ (2007) page 24).

The rejection of Claims 1-21 under 35 U.S.C. 103(a) as being unpatentable over Lipari et al. (U.S. Pat. # 6,232,333) in view of Bailey et al. (U.S. Pat. # 6,008,228) is maintained.

14. Claims 26-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipari in view of Bailey as applied to claims 1-21 above, and further in view of CUBoulder Organic Chemistry Undergraduate Courses, Lab Techniques.

Applicant's arguments see Pages 17-19, filed 09/14/2007, have been fully considered and are not persuasive. Applicant's arguments against the prior art rejection of record are centered on the fact that evaporation is required for concentrating the ritonavir to avoid precipitation and result in a final desired concentration of the active ingredient in the final composition.

This is not persuasive as there is no disclosed critical specific final concentration or final product in the claims and as addressed above and in the previous action. Additionally, as addressed in the previous action, vacuum distillation is a known elementary technique to reduce solvents from a mixture without damaging the product, thereby concentrating the mixture. It is a known technique and obvious for one of skill in the art to do at the time of the invention, as the technique is taught in high school and college. The results of ordinary innovation are not subject to patentability.

Conclusion

15. Claims 1-2, 6, 8, 15-17, 19, 21-35 are rejected.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GiGi Huang whose telephone number is (571) 272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER